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The quest for optimal antimicrobial therapy

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Chapter VII

General Discussion

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This thesis evaluates the development of an implementation program to strengthen the antimicrobial policy of a university hospital. The main goal of that program was to bring prescribing behaviour more in line with recommendations of the hospital antimicrobial treatment guideline. This guideline is considered the cornerstone of the hospital's antimicrobial policy. The hospital antimicrobial treatment guideline aims to stimulate rational use of antimicrobial agents and guide drug therapy choices for a range of infectious diseases.

The implementation program was divided in different phases following the model by Grol ¹. [see chapter I] In the first phase of the implementation program four main questions were addressed:

- 1) How reliable can adherence to guideline recommended therapy be assessed, and by whom?
- 2) What barriers and facilitators exist to following guideline recommendations by physicians in a university teaching hospital in the Netherlands?
- 3) Can non adherent prescribing be attributed to specific patient-groups, e.g. who are more severely ill or have specific co-morbidities?
- 4) Do guideline recommended antimicrobial agents offer sufficient coverage for infective micro-organisms as compared to the frequently prescribed fluoroquinolone ciprofloxacin?

Based on the findings from this initial phase of the study an intervention strategy was selected and developed as phase 2. This intervention strategy combined two elements; an active distribution of the updated guideline among physicians, followed by academic detailing sessions. In the academic detailing sessions feedback of aggregated and individual prescribing data were used. Clinical data and *in-vitro* bacterial culture and sensitivity test results were also studied to underline the reliability of the guideline recommendations for empirically treating infections.

In phase 3 the impact of the combined intervention strategy on prescribing adherence and the additional impact of academic detailing were evaluated.

Assessing the quality of antimicrobial therapy and guideline adherence

We studied the reliability of assessing prescribing quality by professionals from different medical backgrounds. Assessment of prescribing in line with guideline recommendations was guided by an algorithm to assess aspects of antimicrobial therapy stepwise. [Chapter II] We found that adherence of prescriptions to antimicrobial treatment guideline recommendations can be reliably assessed for the choice of drug. To do so, assessors, - internists or hospital pharmacists, - need clear instructions. More extensive training may be needed for a reliable assessment of duration of therapy,

dosage, and route of administration, as well as assessment by other professional groups. The availability of more explicit guideline recommendations facilitates agreement between assessors. In case of dosage or route of administration the guideline lacked such explicit recommendations; it suggested a range of options, leaving room for more clinical judgment on a case-by-case basis.

Volume of antimicrobials used and drug costs are indicators that are used to reflect physicians' prescribing behaviour. These indicators become more meaningful when they incorporate or consider more qualitative information, such as reference to guideline recommendations, patient-, and disease-characteristics, or culture and sensitivity test results. Appropriateness of therapy or adherence to guideline recommendations are such indicators for antimicrobial therapy and are referred to as prescribing quality indicators. Traditionally, indicators are used that merely describe the quantity or volume of antimicrobial agents dispensed or prescribed, these are then referred to as comparators. Such comparators give much less detailed information on the prescribing process ². Choosing adherence to guideline recommendations as outcome measure gives more valuable information of physicians' decision making in a setting where local guidelines exist. As a drawback the reliability of these prescribing quality indicators depends on the assessment procedure and should ideally be validated. Researchers have chosen different approaches tackling the issue of reliability of their outcome parameter. Gyssens *et al* chose to base her analysis on the judgments made by the most experienced assessor, and Ansari *et al* chose to use routine pharmacy data (comparators) instead of having someone to assess adherence to guidelines or appropriateness of antimicrobial therapy ^{3,4}. In this thesis we have chosen for a prescribing quality indicator, using data collected from patient-charts, but limited ourselves to assessing drug choice. In chapter II we show that a reliable assessment of this outcome measure is possible. It is also a relevant outcome measure as non-adherence or inappropriate prescribing occurs primarily with regard to the drug choice, and to a lesser (but not unimportant) extent to dosage, route of administration, or duration of therapy ^{3,5}.

In this thesis quality of prescribing behaviour is assessed with a patient oriented process indicator. This prescribing quality indicator measures the extent to which antimicrobial prescribing is in line with the guideline recommended drug choice, taking into account patient - e.g. age, sex, co-morbidities -, disease -e.g. diagnosis, causative pathogens, severity of disease -, and drug-characteristics. Quality of care for infectious diseases however is more than assessing prescribing behaviour. Hygienic measures are also relevant. The preferred indicator for quality of care therefore would have been a clinical outcome, e.g. mortality, length of stay, or cure-rate. Interpretation of changes in these clinical outcome indicators cannot only be considered in the light of changes in

prescribing behaviour. Changes in hygiene measures, antibiotic policies, presence of co-morbidities in the treatment groups, occurrence of epidemics may all have an effect on these clinical outcomes. Thus interpreting these clinical outcomes demand a focused approach, looking in detail into the impact antimicrobial control programmes have on specific well defined patient and disease cases.

Thus, the advantage of the prescribing quality indicator used in our study is that it is directly related to physicians' prescribing behaviour.

Physicians and their guidelines

Three chapters (III – V) are devoted to unravelling adherence and non-adherence to antimicrobial policies or guideline recommendations. In these chapters we report on barriers and facilitators to using guidelines, and on determinants of (non-) adherence.

Barriers and facilitators

The hospital guideline was *not* very well known by the physicians in our hospital. Those physicians who were aware of the guideline felt the guideline was *outdated*; it was more than 2 years old. A periodical review of guidelines, e.g. every two years, has been repeatedly recommended in the literature. Not only to incorporate the latest evidence, but also to increase acceptability by the target group ⁶. A solid evidence base for the guideline recommendations may be as important ⁷, and has been shown to strengthen the acceptance of guideline recommendations ⁸. Specialists felt not really involved in the development of the guideline. Such lack of *ownership* has been shown to be an important barrier for creating support by the target group for the proposed guideline ⁹.

We found that in a teaching hospital setting, residents were not independent decision makers. Supervisors were more reluctant to use the guideline fearing to lose some of their *autonomy*. The interaction between supervisors and residents has a major impact on residents' prescribing behaviour. Junior physicians, who have freshly finished medical school, were previously shown to prescribe more narrow-spectrum antimicrobials for acute sinusitis. When, however, they started working in a hospital setting they started to copy the prescribing behaviour of their supervisors and slowly changed to use more broad-spectrum agents ¹⁰. Supervisors, thus, function as role models but may not always transfer or develop ideal professional values, behaviour and attitudes in young physicians ^{11;12}. Physicians after finishing medical school are lacking knowledge and skills to handle specific second-line antibiotics or treating nosocomial infections. During their residency they start learning from, and copying, their supervisor's prescribing behaviour for newly learned nosocomial infections. Possibly, this increased experience with second-line antibiotics may lead to their inappropriate

use for “first-line” or ambulatory care kind of infections. Interventions aimed at improving prescribing behaviour in a teaching hospital setting should therefore approach both residents and supervisors.

We assume that to be on the safe side, physicians are treating their current patients with fashionable and overly broad-spectrum agents. In our hospital setting, residents stated to be reluctant to streamline initial broad-spectrum antimicrobial therapy to a narrower spectrum agent, expressing not wanting to “change a winning team”, i.e. clinically effective broad-spectrum therapy. However, implicitly or unknowingly physicians accept possible treatment failure in future patients, because of emerging bacterial resistance.

From the literature many principle barriers can be identified that hamper physicians to follow guideline recommendations. Knowing these factors will provide valuable cues for selecting the appropriate intervention strategy in ones own hospital setting. In our study we identified commonly identified issues as a lack of ownership, out-datedness of the guideline, and physicians fear for less autonomy as relevant barriers to implementing guidelines. More specific local or new problems identified were inefficient dissemination strategies, the resident-supervisor relationship, routine prescribing, and a problem in interpreting bacterial culture and sensitivity test results and whether streamlining of therapy is safe. We than developed a *tailored* intervention that addressed these key-issues to guideline non-adherence.

Pharmaco-therapy committees or hospital boards regularly will intend to strengthen an existing or to develop a new antimicrobial hospital policy. A practical advice would be to involve stakeholders regarding their views on infectious disease management in general, on the current antimicrobial policy, and on the available guidelines. A methodological advice for a scientifically oriented intervention study would be that qualitative studies, such as in-depth interviews, are well suited and can be performed easily to analyze the setting and target group in an implementation program. A more quantitative approach, with e.g. an elaborate questionnaire send to all physicians or relevant staff in order to get a picture of the ‘communis opinio’ on the specific guideline and intended intervention, will not always be necessary. [see Chapter I]

Determinants of prescribing (non-) adherence

Secondly, we looked at the role of patient characteristics in relation to the antimicrobial drug choice considering the availability of bacterial culture results. Patient characteristics were relevant for prescribing in line with recommendations only for a limited number of characteristics. Defensive behaviour, prescribing unduly broad spectrum agents, a fear of using nephrotoxic antibiotics and preference for some drugs seemed to guide physicians prescribing. [Chapter IV & V] Supervisors stated that

routine behaviour plays a role in treating infectious diseases. [Chapter III] This practice is also reflected in the study presented in chapter V, where predominantly one broad spectrum antimicrobial agent was prescribed to treat patients with urinary tract infections (UTI). Contradicting guidelines on national or international level interfered with adherence to local guidelines too. Compliance to guideline recommendations differed considerably between and within the groups of infections studied, compliance was much higher for LRTI than for sepsis and UTI. Denig *et al.* showed earlier that prescribing behaviour of physicians in hospital settings could not be explained by clinical reasoning only ¹³. Social interaction, clinical experience, and following the routine were identified as being important too. We show that for treating infectious diseases this routine may be important too.

Microbiological culture results and adherence

In chapter IV we showed that guideline recommended empirical therapy, often with narrower spectrum antimicrobial agents, covered *in-vitro* cultured pathogens equally well as the much used broad-spectrum agent ciprofloxacin.

This implies that the guideline gives sound advice. But still ciprofloxacin is initially used to a large extent in empirical therapy.

Thus, narrow antimicrobial therapy directed to expected sensitivity patterns of pathogens using local guideline recommendations can be safely prescribed, provided that therapy is narrowed or broadened to culture- and sensitivity test results once these are available.

A remarkable finding is that in a minority of cases even with *in-vitro* culture and sensitivity test results available, physicians still started or continued antimicrobial therapy for which the cultured pathogen was insensitive. Availability of culture and sensitivity test information alone has, as also found elsewhere, proven to be insufficient in changing physicians' prescribing behaviour ¹⁴. Antimicrobial therapy in this retrospective study in four university hospitals was not streamlined in 70 out of 102 cases where this practice was appropriate ¹⁴. This may be attributable to:

a) a lack of self-efficacy of residents. Self-efficacy denotes that physicians feel certain enough they can perform specific tasks. In this case junior residents expressed having difficulties in interpreting what to do with gram-stain and bacterial culture- and sensitivity results.

b) Routine behaviour, as described in the paragraph on determinants of prescribing (non-) adherence (Chapter V), and a reluctance to change an initiated effective therapy for clinical ("never change a winning team") and practical reasons.

However, clinical efficacy may also be explained by the fact that many infections will follow the natural cause of being *self-limited*. From the interviews we know that some

physicians claim that the additional work involved with a new prescription is not worthwhile for sometimes short remaining therapy durations. With the large majority of bacterial culture and sensitivity test results available within three days this is not an acceptable argument ¹⁵. Therefore these arguments are no excuse for continuing inappropriately prescribed antibiotics.

Unsettling as these findings are in a teaching hospital such behaviour might be understandable where it concerns (junior) residents. Though, it appeared from the interviews (chapter III) that also supervisors did not perceive the additional work involved in streamlining to be worth the while. Additional education aimed at residents seems warranted especially addressing this lack of self-efficacy. A recently published survey conducted in Johns Hopkins university teaching hospital (Baltimore, USA), showed that residents scored very low on a knowledge test of antimicrobial therapy for infectious diseases, which did not appreciably improve throughout their years of training ¹⁶. This study suggests that a thorough review of the educational program on antimicrobial therapy and infectious disease for residents is warranted.

Additionally, support will be necessary to physicians for streamlining antimicrobial therapy once test results become available. The adagio of treating infectious diseases should be;

- 1) take appropriate culture samples, preferably before starting empirical therapy,
- 2) check test results,
- 3) stop, change, or continue therapy based on these test results and clinical picture.

Studies performing intervention programs addressing the issue of streamlining antimicrobial therapy had varying degrees of success. In one prospective intervention study, that stimulated physicians to reassess empirical therapy after three days, a tendency to a faster modification of therapy was shown. Though, when the authors explored their data further they found no improvement in streamlining practices in the intervention group ¹⁷. Another recently published intervention study aimed to improve the process of antibiotic therapy in Nijmegen university hospital, the Netherlands. Timing, dose adjustment to renal function, streamlining and switching IV to oral therapy were addressed. The authors, however, found that streamlining during the pre-intervention period was already optimally performed, therefore no intervention was necessary¹⁸. The authors contribute this finding to regular unsolicited consultations by infectious disease specialists in case blood cultures become positive. They also mention the continuing medical education program of residents on this topic. It could be added that in this hospital infectious diseases may be more a focal point of the residents' education program than elsewhere in the Netherlands. Nijmegen has a large infectious diseases department with the head of the internal medicine department, who is also the certified internist-educator, being an infectious disease specialist

Antimicrobial resistance surveillance and improved rapid diagnostic testing are regarded as important instruments that will offer ‘real time’¹ support for optimally targeting initial or ‘empirical’ antimicrobial therapy¹⁹⁻²³. However, those developments need support to be picked up by prescribers. Feedback of susceptibility data alone seemed in the past to be not very effective²⁴.

Improved and fast diagnostic testing to guide the *initial* –‘empiric choice’– will have a great potential to optimize therapy. Improving *initial* therapeutic decision making has the potential for the largest quality gain, especially in view of the fact that physicians tend to stick to their initial therapeutic choice. Inexperienced physicians will need support for interpretation of culture and sensitivity test results and *all* physicians need to be stimulated to streamline therapy based on these results.

Improving adherence

Armed with this knowledge on physicians’ barriers to following guideline recommendations in daily clinical practice a tailored intervention strategy was developed. The strategy combined two elements; an active distribution of the updated guideline followed by academic detailing sessions. The guideline was updated based on a review of the existing evidence base, available antimicrobial treatment guidelines, and local resistance patterns. The target group was actively involved, to improve a sense of *ownership*. The guideline was actively disseminated in paperback format and was made available, as a searchable PDF-document, on the intranet. In plenary meetings of the department of internal medicine and pulmonology the guideline was introduced in a lecture on antimicrobial use. After a five-month interval academic detailing sessions were initiated, combined with feedback of aggregated and individual prescribing data, and data on the reliability of the guideline recommendations for empirically treating infections. Both residents and supervising specialists were addressed.

Updating the guideline in close collaboration with the targeted specialists followed by active dissemination led to an immediate 16% improvement of adherence. [Chapter VI] Generally, simple distribution of guidelines does not lead to improved prescribing^{25;26}. Our study suggests that improving ownership and ensuring easy access to the guideline information strongly contributes to the use of revised guidelines. Finally, a stable 86% adherence level is reached post-intervention. Five-months of academic detailing sessions had a limited additional impact on prescribing adherence. A ceiling effect may have contributed to this. Apparently we had reached an optimal / maximal adherence level. Guidelines cannot be expected to be specific enough for all clinical cases.

¹ ‘Real time’ is an information technology term used to describe actions or information flows that happen or are available instantly.

Although, initial adherence to guideline recommendations was relatively high (67%), this may have been caused mainly by limiting assessment to drug choice alone. This limitation was made as assessment of drug choice alone was more reliable than assessment of all aspects, dosage, duration of therapy, and administration-route, of the Kunin-Gyssens algorithm of antimicrobial therapy ^{27,28}. [Chapter II]

Recently, doubts were cast on the evidence base of the assumed effectiveness of (combined) interventions ^{26,29}. Unravelling the impact of the different components of an intervention strategy may help to solve this issue. Our study is executed in line with this debate on effective interventions. It analyzes sequentially the different intervention components using a robust quasi experimental analysis technique –an interrupted time series study design analyzed with segmented linear regression – following EPOC criteria ³⁰.

Cost savings by increased adherence as shown by other authors could not be reproduced in our study. A shift in drug use, a somewhat increased overall antibiotic use and incidental extremely expensive individual patient-treatments with systemic antifungal agents contributed to an erratic pattern of antimicrobial therapy costs during the study period. Following guideline recommendations does therefore not necessarily mean that treatment costs will diminish.

Recommendations

When setting out to improve antimicrobial use in hospital care a stepwise approach can guide one successfully through the implementation program ¹. Using the model by Grol as in this study, or employing any plan-do-study-act, (PDSA)-cycle, will help to target the intervention to suit the local situation ³¹. When it is intended to study the impact of one's intervention a rigorous study design should be used ^{29,30}.

Below, various recommendations will be proposed to improve antimicrobial therapy and maintain the impact of an intervention program.

Development of guidelines

Paying continuous attention to credibility and acceptance of the guideline recommendations by the target group is of paramount importance. This can be achieved by person-to-person meetings with key-figures of involved hospital departments. Though this is a known phenomenon⁹, it needs to be implemented and sustained in real life. It is advisable to make someone primarily responsible for this task, as a spokesperson for an antimicrobial committee or infectious diseases department.

To increase the credibility of antimicrobial treatment guidelines it is important to keep recommendations up-to-date by visibly incorporating local antimicrobial resistance patterns and the latest evidence base.

A good instrument is available for critically assessing updated and existing guidelines in the Appraisal of Guidelines for Research and Evaluation in Europe (AGREE)³². The main AGREE-criteria a good guideline has to meet are:

- 1) a clear definition of the problem the guideline is intended to cover,
- 2) involvement of the stakeholders in developing the guideline ,
- 3) recommendations based on a rigorous and transparent systematic review of the literature,
- 4) explicit recommendations supported by evidence,
- 5) external reviewed,
- 6) recommendations applicable to daily clinical practice,
- 7) an independent editorial board.

The local hospital antimicrobial treatment guideline has problems complying with these criteria. The stakeholders, internists, perceive to be not sufficiently enough involved in developing the guideline. Though the guideline recommendations are based on the available evidence, no formal systematic literature review is undertaken. Neither is this review of the literature made very transparent outside the pharmaco-therapeutic committee that drafts the guideline. Only limited external review takes place and there is no independent editorial board. In our implementation program especially the involvement of the stakeholders was improved.

Probably, for most locally developed antimicrobial treatment guidelines in hospitals it is difficult to meet all these criteria due to personnel or time-constraints³³. But this does not discharge hospital therapeutic committees from carefully developing and regularly updating local guidelines and sufficiently involving the relevant stakeholders. In the Netherlands, the Dutch Working Party on Antibiotic policy (Dutch acronym is SWAB)² has adopted at the national level a rigorous process for development of antimicrobial treatment / infectious disease guidelines, based on the AGREE-format. [<http://www.swab.nl>] Local guidelines would benefit from closely following such national guidelines. Deviations from national and international evidence based guidelines should be supported by local bacterial resistance patterns. A further selection

² The major goal of the SWAB is to contribute to the containment of the development of antimicrobial resistance and of the expanding costs of the use of antibiotics. This is achieved by optimizing the use of antibiotics by means of guideline development, education and antibiotic resistance surveillance.

of comparable appropriate antimicrobials for specific indications can than be made on cost considerations and local preferences.

Dissemination of guidelines

Active, including person-to-person, distribution of a credible guideline contributes to an improved use of that guideline. In patient-reports, clinical conferences, regular departmental meetings, continuous medical educational meetings, etc. the guideline or updates should be brought to attention of the clinical staff. Using modern communication devices, such as personal digital assistants (PDA's) and making guidelines available on the hospitals' internal computer network, improve the accessibility of those guidelines. Intranet use has a very low threshold in a middle-sized Dutch hospital in the first year of availability the pharmacy website had 13,000 hits ³⁴.

Keeping guidelines up-to-date and used properly

A dedicated staff member, e.g. a junior pharmacist, could be appointed in teaching hospitals to support an antimicrobial management team (AMT). Essential is that someone is primarily responsible, but could be junior physicians with an interest in infectious diseases or clinical microbiology too. This professional should keep in touch with prescribing habits, perception of physicians towards the guideline, and needs in the departments to ascertain acceptability of the guideline. Such a professional can function as the intermediate between clinical care physicians and the core members of the pharmaco-therapeutic committee members. In the UK a specialized antibiotic pharmacist is employed in an increasing number of hospitals ³⁵. They have a key role in educating medical, nursing and pharmacy staff, monitoring of antibiotic consumption, formulary development, they participate in infection control and appraisal of new medicines. The antibiotic pharmacists function next to infectious disease specialists and clinical microbiologists. In the UK further expansion of the role of these pharmacists is envisioned, moving from an advisory function to a more active direct role in prescribing decisions ³⁵.

Developing a good surveillance system to monitor the impact of antimicrobial use on local bacterial resistance patterns is important to adapt where necessary guideline recommendations. Surveillance data can also be used to support guideline use, because of underlining the need of prudent antimicrobial use ³⁶. Again, the dedicated antimicrobial staff member could be instrumental in monitoring and stimulating the use of the available culture-test information.

Timely adaptation of guideline recommendations should be made based on surveillance data, availability of important new treatment options, or current developments (e.g.

SARS or MRSA outbreaks). Changes in guideline recommendations can be quickly made when such guidelines are electronically available, as on the intranet.

Data on adherence

Sufficient training should be given to assessors before they will be able to give a reliable and consistent assessment of adherent prescribing behaviour to guideline recommended antimicrobial therapy. A reliable assessment of adherent prescribing is not only necessary for internal validity of the presented data but also for the credibility with the target group. Physicians will accept feedback on their prescribing performance better, when the indicator considers relevant and information-rich clinical data.

Challenges for the future

Maintaining high levels of adherence to guideline recommendations in the hospital setting is not self-evident. Major efforts are needed to maintain the relatively good position of the Netherlands with respect to antimicrobial use and bacterial resistance. Routine monitoring of antimicrobial process outcomes supported by information technology developments should be undertaken to signal problem areas. Automatic data collection with e.g. Computerized Physician Order Entry (CPOE) systems, and Electronic Patient Dossiers (EPD), facilitate this process. Appropriate, timely and meaningful analyses of such routinely available data sources and their implementation in daily clinical practice will be the challenge for the future.

Policy-makers will be interested in monitoring expenditures and cost-effective prescribing for specific indications. Here, indicators of prescribing and resistance patterns will need to be robust and validated to allow for useful (inter)national comparisons. Sustainable and reliable data-retrieval is the primary focus of the European projects, ESAC and EARSS, for respectively collection of antibiotic use and resistance data ³⁷⁻³⁹. The signal function from the collected data should then be used to direct European and national antimicrobial policies and health care funding in ambulatory and hospital care.

Professionals will be interested in more detailed indicators of prescribing quality and resistance. These professionals will also be interested in signals of changing or emerging regional resistance patterns. Preferably, *real time* detailed data should be available to support physicians' current prescribing decisions. Experienced specialists should be given readily access to detailed prescribing and resistance patterns and be thoroughly involved in antimicrobial policy and guideline developments. Infectious disease specialists but also 'antimicrobial' pharmacists working together in antimicrobial

management teams can convey educational and managerial infectious disease issues to train and support insecure junior physicians treating infectious diseases.

Developing and testing computer algorithms incorporating data on bacterial resistance, therapeutic guidelines, and clinical patient characteristics for *decision support systems* will be a next step once these CPOE and EPD systems become common place in clinical practice. These decision support systems are than one other tool available in the quest for the optimal antimicrobial therapy.

Prescribing quality indicators derived from these advanced data-sources can also be used to measure the impact of programs or policies aimed at improving antimicrobial prescribing behaviour. The routine monitoring of data-rich prescribing quality indicators, including clinical outcome data, coupled to advanced registration of resistance patterns will give hitherto unavailable, insight in the causal relation of antimicrobial prescribing practices, bacterial resistance and clinical outcome. The outcome measures bacterial resistance and clinical outcome complement the interpretation of process outcome prescribing quality indicators; such as adherence to guidelines as employed by us. Whereas process indicators show whether antimicrobial control measures in the hospital are being picked up, there is an increasing need for clinical outcome and bacterial resistance data. These data will enable us to demonstrate that we are safely and effectively treating our patients and not just 'squeezing the resistance balloon at one end' ⁴⁰. Meaning that by replacing specific antimicrobials for others, through means of guidelines, antimicrobial cycling or formulary restrictions, bacterial resistance shifts from one agent to the other.

Thus, keeping in mind the central role of the ward physician, managing infectious disease is increasingly becoming an area of shared care. Dedicated staff members, all or not attached to multidisciplinary antimicrobial management teams, focus on antimicrobial policy issues. They will be instrumental in maintaining high levels of prescribing quality. These AMT members will be needed to fully utilize and embed newly developed diagnostic and prescribing support tools in daily clinical practice. In this quest for optimal antimicrobial therapy ward physicians should probably remain primary responsible in treating infections, but will more than occasionally need support to succeed.

Final conclusion

Antimicrobial prescribing behaviour in hospital care can be influenced with a variety of different intervention strategies. When a tailor made intervention strategy is used that is based on a careful analysis of existing barriers and prescribing behaviour, non-compulsory measures can lead to a large gain in prescribing adherence. Thus simple interventions, such as improving the credibility and actively disseminating an existing guideline, can lead to improved prescribing adherence. Labour intensive interventions such as academic detailing may then not be strictly necessary or can be reserved for especially costly inappropriate antimicrobial use, e.g. new drugs.

Future efforts in strengthening antimicrobial policies should be a combination of:

- 1) making someone responsible – appointing a dedicated antimicrobial staff member –,
- 2) involving all stakeholders,
- 3) strong multi-departmental cooperation,
- 4) regularly updating the guidelines plus active dissemination,
- 5) optimal utilization of increasingly advanced information technologies, including their possibility to generate high quality feedback data on antibiotic consumption and bacterial sensitivity patterns.

Abundantly clear is that continuous efforts are needed to maintain high standards of pharmacotherapy for infectious diseases;

... the *quest for optimal antimicrobial therapy* never ends.

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